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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/857,719	12/03/2001	Ryuichi Morishita	6235-59216	9622

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EXAMINER	
LI, QIAN JANICE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/857,719	MORISHITA ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,12,14,16,18,33 and 36-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12,14,16,18,33 and 36-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *03 December 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response filed on 6/17/03 and supplemental amendment filed 11/10/03 have been entered. Claims 1-10, 13, 15, 17, 19-32, 34, 35 have been canceled. Claims 11, 14, 16, 33 have been amended, and claims 36-41 are newly submitted. Claims 11, 12, 14, 16, 18, 33, and 36-41 are pending in the application and under current examination.

Specification

Applicants failed to respond to the following matter raised in the previous Office action, thus the objection stands as follows.

> The Preliminary amendment requested insertion of a paragraph starting with "WE CLAIM" on page 11, however, page 11 contains the text of the specification, and it is improper to insert the claims there. The original page for claims starts at page 13.
> Appropriate clarification is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11, 12, 14, 16, 18, 33, stand rejected and claims and 36-41 are newly rejected under 35 U.S.C. 112, first paragraph for reasons of record and following.

In the 6/17/03 response, applicants argue that the specification taught several exemplary HGF molecules and other non-HGF polypeptides, thus, enables the instant

claims. Applicants also amended claims to recite directly administering a therapeutic amount of a nucleic acid molecule to a part of an affected cardiac muscle of a mammal using echocardiographic guidance without thoracotomy.

The argument has been fully considered but they are not persuasive for reasons of record and following.

Claims are drawn to therapeutic methods for treating myocardiopathy and/or any tissue of any disease, which requires achieving a therapeutic effect for treating diseases. However, other than HGF-HVJ-liposome, the specification fails to teach any significant gene transfer for any other nucleic acids or polypeptides to any tissue other than the heart, it fails to teach any therapeutic effect for any disease for the broadly claimed nucleic acids and therapeutic polypeptides, whether it is using local administration or systemic administration. The prophetic teaching of the specification fails to teach how to overcome the art known hurdles in gene transfer and therapy as taught by *Robbins et al*, *Miller et al*, and *Deonarain,* thus, fails to provide sufficient enabling disclosure for practicing the invention without undue experimentation.
It is noted that claim 16 encompasses using any polypeptide, far broader than the few polypeptides contemplated in the specification, claim 36 encompasses delivery to any tissue including tissues remote from the heart, which requires gene targeting, and encompasses delivering to any tissue for treating any disorder guided by an echocardiography. However, the specification is silent and fails to teach how and the efficiency of such approach. Claim 37 recites "using echocardiographic guidance without an incision", if this is an inventive concept, there ought to be more teachings

regarding the procedure, however, the specification is as brief as the claim, it is unclear what the claim encompasses or excludes. Applicants are reminded that the specification must teach those of skill in the art how to make and how to use the invention as broadly claimed. In re Goodman, 29 USPQ2d at 2013 (Fed. Cir. 1994), citing In re Vaeck, 20 USPQ2d at 1445 (Fed. Cir. 1991); and that 35 U.S.C. § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. In re Fisher, 166 USPQ 18, 24 (CCPA 1970). The instant specification fails to meet these criteria for providing an enabling disclosure.

New claims 38-41 clarify the effect of expressing the delivered polypeptide, do not provide further enablement for the original rejected claims.

Accordingly, in view of the quantity of experimentation necessary to determine the parameters for achieving *in vivo* gene targeting at therapeutic levels, in particular for the treatment of any and all myocardiopathy, any and all diseases, the lack of direction or guidance provided by the specification, and the breadth of the claims directed to the use of numerous nucleic acid molecules in combination with any type of therapeutic polypeptides, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Previous rejections under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendment.

Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

Claim 37 is vague and indefinite because Claim 37 recites "using echocardiographic guidance without an incision", the specification fails to teach the meaning of the "incision", it is unclear what the term includes or excludes, for example whether placing a catheter is considered having an incision, thus the metes and bounds of the claim is unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (f) he did not himself invent the subject matter sought to be patented.

Prior rejection of claims 1-12, 15, 26-29, 32, 34, and 35 under 35 U.S.C. 102(e) as being anticipated by *Morishita et al* (US Patent No. 6,248,722) is withdrawn in view of claim amendment.

Prior provisional rejection of claims 1-12, 15, 26-29, 32, 34, and 35 under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/660,522 is withdrawn because the cited application is now abandoned.

The prior provisional rejection of claims 1-10, and 26-28 under 35 U.S.C. 102(e) as being anticipated by copending Application No. 09/856,374, is withdrawn because the rejected claims have been canceled.

The prior rejection of claims 1-12, 15, 26-29, 32, 34, and 35 under 35 U.S.C. 102(f) in reference to US Patent No. 6,248,722 is withdrawn in view of claim amendment.

The prior provisional rejection of claims 1-12, 15, 26-29, 32, 34, and 35 under 35 U.S.C. 102(f) in reference to copending Application No. 09/660,522 is withdrawn in view the abandonment of the cited application.

The prior provisional rejection of claims 1-10, and 26-28 in reference to copending Application No. 09/856,374 under 35 U.S.C. 102(f) is withdrawn because the rejected claims have been canceled.

The prior rejection of claims 1-12, 15, 26-29, 32, 34, and 35 under 35 U.S.C. 102(b) as being anticipated by *WO 97/07824* is withdrawn in view of claim amendment.

The prior rejection of claims 8 and 9 under 35 U.S.C. 102(b) as being anticipated by *Hammer et al* (US 5,792,453) is withdrawn because the rejected claims have been canceled.

The prior rejection of claims 8 and 9 under 35 U.S.C. 102(b) as being anticipated by *Esakof et al* (Hum Gene Ther Sept 1999;10:2307-14, IDS) is withdrawn because the rejected claims have been canceled.

The prior rejection of claims 8 and 9 under 35 U.S.C. 102(b) as being anticipated by *Maurice et al* (J Clin Invest Jul 1999;104:21-9) is withdrawn because the rejected claims have been canceled.

The prior rejection of claims 8-10 under 35 U.S.C. 102(b) as being anticipated by *Aoki et al* (Circulation 1998;98:I321, IDS) is withdrawn because the rejected claims have been canceled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

In view of claim amendment, the rejection under this section has been modified as following.

Claims 11, 12, 14, 16, 18, 33, and 36-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over *WO 97/07824, Esakof et al* (Hum Gene Ther 1999

Sept;10:2307-14) and *Maurice et al* (J Clin Invest 1999;104:21-9), further in view of *Stevens et al* (US 5,916,193).

The amended claims are drawn to using a catheter under the guidance of echocardiography without thoracotomy or an incision to deliver a nucleic acid molecule to cardiac tissue.

As discussed in detail in the previous Office action, the combined teachings of *WO 97/07824, Esakof et al* and *Maurice et al* teach delivering a nucleic acid encoding a gene of interest to myocardial tissue through a catheter guided by the transesophageal echocardiography during the open-heart procedure, but fail to teach using a catheter without thoracotomy.

However, before the instant effective filing date, *Stevens et al* teach a venting catheter system for accessing heart anatomy without the need for a thoracotomy (abstract). They teach the advantage for using such catheter system for a heart procedure without a thoracocotomy, "THEREBY REDUCING MORTALITY AND MORBIDITY, DECREASING PATIENT SUFFERING, REDUCING HOSPITALIZATION AND RECOVERY TIME, AND LOWERING MEDICAL COSTS RELATIVE TO PREVIOUS OPEN-CHEST PROCEDURES" (column 5, lines 56-67). They go on to teach that accurate placement of the catheter could be verified by fluoroscopy or transesophageal echocardiography (column 13, lines 25-27 and column 20, lines 13-24).

New claims 36 and 37 encompass claim 11, new claims 38-41 state the intrinsic tissue effect of the delivered nucleic acid molecule as a result of protein expression, thus are taught by the combined teachings.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *WO 97/07824, Esakof et al*, and *Maurice et al* by adopting the catheter system taught by *Stevens et al* in the nucleic acid cardiac delivery procedure with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the method because it provides a safe and cost-effective means for transgene delivery. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

The prior rejection of claims 11-13, 16-18, 30, 31, and 33 under 35 U.S.C. 103(a) as being unpatentable over *WO 97/07824,* in view of *Hammer et al* (US 5,792,453) is withdrawn in view of claim amendment and argument.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Prior rejection of claims 11, 12, 15, 29, 32, 34, and 35 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 4-6 of U.S. Patent No. 6,248,722 is withdrawn in view of claim amendment.

The prior provisional rejection of claims 11, 12, 15, 29, 32, and 33 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7 and 8 of copending Application No. 09/660,522, in view of *Maurice et al* (J Clin Invest 1999;104:21-9) is withdrawn because the cited application has been abandoned.

The prior provisional rejection of claims 1-10, and 26-28 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent Application Serial No: 09/856,374 is withdrawn because the rejected claims have been canceled.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942 (571-272-0730, after the Office relocation in January, 2004). The examiner can normally be reached on 9:30 am - 6 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Q. Janice Li
Patent Examiner
Art Unit 1632

QL
December 9, 2003

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER